Highly Enantioselective Hydrogenation of Methyl Acetoacetate catalyzed by Tartaric Acid-NaBr-Modified Raney Nickel under Low Hydrogen Pressure

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Abstract: Enantioselective hydrogenation of β-ketoesters over tartaric acid-NaBr-modified Raney nickel has been studied intensively at a high H_2-pressure, typically, using methyl acetoacetate (MAA) as a standard substrate (86 %ee at 10 MPa). It is shown here with MAA, for the first time, that high enantio-excess of methyl 3-hydroxybutanoate (92 %ee) can be achieved even under low H_2-pressure (0.05-0.5 MPa) at 333K, this extending industrial usage of the catalyst system. Reaction kinetics were also studied at both low and high H_2-pressure to understand the origin of enantioselectivity, combined with DFT calculations, suggesting that strong interactions between surface tartaric acid-substrate are beneficial for high ee.

Keywords: Enantioselective hydrogenation of ketones, Raney nickel, Low hydrogen pressure.

1. Introduction

Tartaric acid-modified Raney nickel (TA-MRNi) is currently one of the most feasible and industrially applicable catalysts for enantioselective hydrogenation of prochiral ketones because of its easy handling, separation and rejuvenation. However, the hydrogenation requires high H_2-pressure (usually 10 MPa) to ensure high optical yields. It has been shown that the enantioselectivity (86 %ee at 10 MPa)[1] of the hydrogenation of methyl acetoacetate (MAA) over TA-MRNi is significantly decreased at lower H_2-pressure (< 2 MPa).[2] On the other hand, Osawa et al. reported 82 %ee at 0.2 MPa of H_2 at 333 K under a high stirring rate.[2] Reducing H_2-pressure while maintaining high optical yield would be a very beneficial option from the viewpoints of hydrogen atom economy and safety. In the present study, we examined catalytic behaviors of the enantioselective hydrogenation of MAA as a standard substrate over TA-MRNi at 333 K under low H_2-pressure (0.05-0.5 MPa) using a reciprocating shaking glass autoclave. We also studied the reaction kinetics at low H_2-pressure to understand the origin of the enantioselectivity over TA-MRNi.

It is assumed without direct evidence that enantioselective hydrogenation over TA-MRNi is induced through the interactions between surface chiral TA moiety and prochiral substrate. Accordingly, selectivity depends on the type of the substrate; 74 %ee for acetylacetone (AA) and 69 %ee for 4-hydroxy-2-butanone (HB) at 333 K and 10 MPa (Scheme 1).[3] In the present study, we tried to obtain deeper insights into the origin of enantioselectivity through the relationship between substrate-modifier interaction strength and enantioselectivity from the kinetics point of view using three types of the substrate, combined with DFT calculations.

Scheme 1. Enantio-differentiating hydrogenation of ketones. R= $-CH_2COOCH_3$ (MAA), $-CH_2COCH_3$ (AA), $-C_2H_4OH$ (HB), $-C_6H_{13}$ (2O)

2. Experimental

TA-MRNi was prepared by heating the RNi at 373 K for 1 h in aqueous solution of TA and NaBr. After the modification, the solution was removed by decantation, followed by thorough washing with water, then with methyl alcohol, and finally with tetrahydrofuran (THF). The enantioselective hydrogenation of MAA was conducted using a reciprocating shaking glass autoclave (Parr Reactor) at 333 K under low hydrogen pressure (0.05-0.5 MPa). The H_2-pressure was kept constant during the hydrogenation. The competitive and individual hydrogenation reactions between MAA, HB, 2O, and AA were conducted at 333 K and 10 MPa of H_2 using a reciprocating shaking steel autoclave without using solvent.

3. Results and discussion

The reactions were conducted at the same initial substrate (MAA) concentration and reaction temperature of 333 K, but under different H_2-pressure (0.05-0.5 MPa). Fig.1a shows that the enantioselectivity is kept very high >87 %ee even at 0.1 MPa, although the selectivity is slightly decreased to 82 %ee at a sub-atmospheric H_2-pressure (0.05 MPa). The ee slightly increased as the H_2-pressure was increased and reached 92 %ee, the highest ee value reported for MAA hydrogenation. It is noteworthy that sufficiently high selectivity can be achieved even at a very low H_2-pressure, when appropriate reaction system is adopted. This makes TA-MRNi more feasible in industrial uses. The reaction rate is shown in Fig.1a as a function of H_2-pressure. It is found that the reaction rate is described using an L-H rate equation. Comparison of the present kinetics results with the hydrogenation over unmodified RNi and TA-modified Ni/SiO_2 will be presented to suggest that the interaction strength between surface TA moiety and MAA is crucial. This point is envisaged by the hydrogenation at 10 MPa, as shown in Fig.1b.

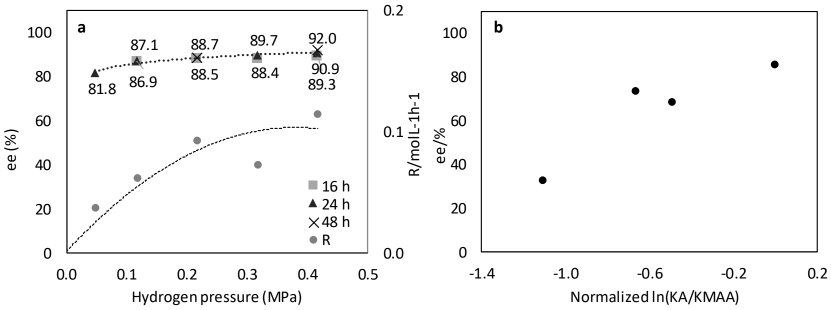

Figure 1. (a) Effect of hydrogen pressure on optical yields of hydrogenation of MAA over TA-MRNi at 333K under low H_2-pressure, (b) Relation between ee and substrate-modifier interaction strength estimated from competitive hydrogenation of ketones over MRNi (both TA modified and unmodified) catalyst at 333 K and 10 MPa.

In the present study, factors determining ee in enantioselective hydrogenation of ketones were examined from the viewpoint of reaction kinetics, for the first time, to understand how functional groups attached to the ketones affect the hydrogenation rate and its enantioselectivity. By comparing the initial rates of both individual and competitive hydrogenations, the relative reaction rate constant and equilibrium adsorption constant of each substrate were evaluated based on an L-H mechanism. In addition, DFT calculations were performed to estimate the adsorbed TA-substrate interaction energies. DFT calculations show that the relative adsorption equilibrium constant K is well correlated to the hydrogen bond interaction energy of the substrate and glyceric acid as a DFT model compound for TA moiety adsorbed on RNi through one of the carboxyl groups. This confirms that the relative adsorption equilibrium constant can be used as a parameter representing the interaction energy. Fig.1b shows that the ee value increases as the relative K value increases. In conclusion, both kinetics results and DFT calculations clearly indicate that the substrate-modifier interaction strength is well correlated with the ee value.

4. Conclusions

Sufficiently high optical yields (up to 92 %ee) can be achieved for enantioselective hydrogenation of MAA over TA-MRNi at 333 K under low H_2-pressure (0.05-0.5 MPa) using reciprocating shaking glass autoclave. This makes TA-MRNi system more beneficial and feasible for industrial application. In addition, kinetic studies of competitive hydrogenation suggest that the substrate affects the substrate-modifier interaction strength and consequently enantioselectivity of the product.

References

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